INTEGRITY IN RESEARCH:
Individual and Institutional Responsibilities

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OBJECTIVES:

1. To provide a historical perspective on the emergence of research integrity as a highly visible, sensitive, and contentious issue among the public (media), Congress, and the scientific community.

2. To discuss the initial responses of scientific institutions and scientists to the integrity issue, and how these responses have evolved.

3. To summarize current administrative and legal procedures concerning research integrity, and the recent report of the National Commission on Research Integrity.

4. To discuss the Guidelines for the Conduct of Research in the Intramural Research Program at NIH.

5. To comment on unresolved aspects of the scientific integrity issue, including, the definition of scientific misconduct, conflict of interest questions, individual versus institutional responsibility, and maintaining scientific creativity.

OUTLINE:

Integrity in Research

I. Evolution of the Issue

- A. Scientific Scandals
- B. Institutional Responses
- C. Media Coverage
- D. Congressional Responses
- E. Federal Regulations - OSI and OSIR; ORI

II. Responses of the Scientific Community

- A. Articles and Symposia
- B. 1989 IOM Report; 1992 NAS/NAE/IOM Report; 1995 CRI Report
- C. Institutional Guidelines
- D. Courses and Textbooks

III. Guidelines for the Conduct of Research in the Intramural Research Program at NIH.

- A. Supervision of Trainees
- B. Data Management
- C. Publication Practices
- D. Authorship
- E. Peer Review and Privileged Information

F. Financial Conflicts of Interest

G. Clinical and Epidemiological Research

IV. Unresolved Issues

A. Definition of Scientific Misconduct

B. Conflicts of Interest

C. Individual versus Institutional Responsibility

D. Maintaining Scientific Creativity

INTEGRITY IN RESEARCH:
INDIVIDUAL AND INSTITUTIONAL RESPONSIBILITIES

During the last decade the subject of integrity in research has become of sufficiently high visibility that there is now no end of meetings, reports, articles, books and courses devoted to this topic. Indeed, formal education in research integrity is now a required of trainees in both the NIH intramural and extramural programs. The fascination of the news media (and presumably the public) and the U.S. Congress with scientific conduct issues has forced the scientific community - and its host institutions and support agencies - to examine carefully our codes of conduct. It is presumably in this context that you are reading this article that I, a working scientist, have prepared in an attempt to put into perspective this difficult topic. It is hoped that this review, in conjunction with the list of suggested readings and the appended text of the NIH Guidelines for the Conduct of Research, will present the reader with a coherent way of understanding the rapidly evolving components of theses issues.

Although many of us believe that we know what the scientific method is and what practices are acceptable in following this method, examination of the history of science suggests that even these considerations involve philosophical disputes that are far from simple, especially with regard to the selection of data and the treatment of apparently contradictory data or alternative concepts. Thus the famous controversies involving handling of data by Sir Isaac Newton, Gregor Mendel, Robert Millikan and many others have been of intense interest to both historians and philosophers of science. The ultimate resolution of these great controversies that, in Thomas Kuhn's

phrase, involve paradigm shifts, as well as more specialized debates, has left many of us with the belief that science is essentially an error-correcting process and that we should not be too concerned with inadvertent or, even, intentional error. Although intentional error was obviously abhorrent it was believed that it was so rare and so likely to be exposed as to be an insignificant problem. For these reasons, neither scientists, their professional organizations, their institutions of employment, nor the government (which funds the major part of research) were prepared for the public reaction to accusations of scientific misconduct that came with increasing frequency after the mid-1970's.

I believe that the first sign that the internal workings of science would be subject to widespread discussion was the media response to the painted mice episode, which occurred during a study of tissue transplantation at the Sloan Kettering Institute for Cancer Research in New York in the mid-1970's. These stories were followed in the next decade by others about apparent falsifications of data or other questionable research behavior at the Massachusetts General Hospital, Peter Bent Brigham Hospital, Massachusetts Institute of Technology, Yale University Medical School, Cornell University, University of California School of Medicine at La Jolla and many other research institutions. It is interesting to note that most episodes were at large, research-intensive institutions in the biomedical sciences.

Although these events received extensive attention from the press, the response of the scientific community and, in particular, the involved institutions was basically to cauterize the wound rapidly - in secret if possible - and to move on. Generally institutional committees formed to investigate

the allegations found that the person accused (almost always a post-doctoral fellow) should be dismissed - sometimes psychiatric therapy was recommended - and that otherwise the senior investigator (usually the holder of a sizable research grant or multiple grants) was absolved of responsibility. In one well-publicized case, the whistle-blower was forced out, and neither the senior investigators nor the institutions would even seriously investigate the episode - a situation that led to an unfortunate series of external reviews lasting almost a decade.

I believe that the philosophy underlying these responses, that the episodes were idiosyncratic results of a few "bad apples" and that the scientific system would self-correct erroneous results, dictated the nature of these initial responses to these very embarrassing episodes. It should also be noted, as will be discussed later, that there were obvious conflicts of interest in these procedures as the senior investigators and the institutions themselves were recipients of tangible and intangible benefits from the continued conduct of the research. This pattern of response would likely have continued to this day except for the increasingly strident responses of the press, Congressional committees and the actions of two scientists at NIH, Drs. Ned Feder and Walter Stewart.

The increased attention in the press coincided with its increased involvement since Watergate in investigational and even adversarial roles, especially with regard to government and government-funded activities. In addition to the change in journalism in general, science reporting was itself undergoing comparable changes. Reporters on major newspapers and magazines now, it would seem, spend as much time reporting controversies

as the scientific results themselves, viz. the “cold-fusion” story. Even journals like Science and Nature have large sections and staffs devoted to the politics and debates affecting science. In particular, the book by William Broad and Nicholas Wade (now on the staff of the New York Times), “Betrayers of the Truth: Fraud and Deceit in the Halls of Science,” with its sensationalist style, from its title on, published in 1982 set the tone, I believe, for much that has followed.

Further, the work of our NIH colleagues Drs. Stewart and Feder pointed out that in several instances of apparent misconduct the acts were part of a general pattern of limited supervision of post-doctoral fellows in very large and well supported laboratories and that this circumstance itself probably contributed to facilitating, or perhaps even promoting (because of competitive pressures), the misconduct. They called for the scientific community to address its own structural problems, as did several other scientists. (The methods of Drs. Steward and Feder, however, resulted in their efforts becoming quite controversial.)

Equally important was the Congressional response to these many episodes. In 1981, then Representative Albert Gore, chaired a review by a Subcommittee of the Committee on Science and Technology of the House of Representatives which articulated concern about the lack of response by the scientific community to problems related to scientific conduct. The NIH Authorization Bill in 1985, probably as a result of these hearings, required for the first time recipients of NIH funds to have administrative processes in place to review allegations of misconduct. On the basis of that legislation, the Public Health Service issued interim Guidelines in 1986 that became the so-

called “Final Rule” in 1989. (The term “Final Rule” is a bit intimidating, but that is its official name.)

Figure 1 summarizes three parts of this 1989 Executive Branch ruling which are important for consideration. First is the still extant definition of misconduct, which is centered around the idea that “fabrication, falsification and plagiarism” (FFP) are the essence of any definition of misconduct in science (or research), with careful sheltering of “honest” error or differences in judgment. However this definition itself has been the object of a great deal of discussion and controversy since 1989 - in particular because of the phrase “other practices that seriously deviate from those commonly accepted within the scientific community,” which I will discuss below. The 1989 ruling did two further things - it created an Office of Scientific Integrity in the Office of the NIH Director (and a Review Office in the Department of Health and Human Services) and it implemented the 1985 legislative suggestion that each PHS-supported institution must have relevant administrative processes in place to investigate allegations of scientific misconduct.

After several stormy years in which scientists tried to manage it in a semi-collegial way, based on the methods of scientific review of data, the NIH Office of Scientific Integrity was renamed the Office of Research Integrity and moved to the Department of Health and Human Services (DHHS) in 1992, with much greater input from lawyers and use of legal procedures and precedents in implementing its work. These procedures included the rights of the accused to cross-examine their accusers and other aspects of “due process”. Although still not free from controversy (which controversy has been lessened somewhat by the recent overturning of several of the Office of

Research Integrity's findings by the DHHS Research Integrity Adjudications Panel), the functioning of this Office appears to have become tolerated, if not fully accepted, by the scientific community.

It should also be pointed out that until now virtually all of the regulations that affect the conduct of research have come not from legislative initiatives but from Executive Branch regulations. However, during the spring of 1989, and for the next several years, the glare of publicity hit the issue of scientific misconduct through the oversight investigations of the House Committee on Energy and Commerce, then chaired by Representative John Dingle. The activities of this Committee, which continued until the change in political control of the Congress at the end of 1994, were devoted to detailed examination of a few prominent cases of alleged scientific misconduct, but also implicitly questioned the adequacy of the Executive Branch regulations and actual investigations, as well as those of the scientific community itself. Of great concern was the possibility that legislation on these matters would ensue.

The initial responses of the scientific community to the scandals of the 1970's and afterwards were generally bland and defensive, beginning with the testimony of Dr. Philip Handler, then President of the National Academy of Sciences, before Representative Gore's Subcommittee in 1981. Gradually, however, the glare of publicity began to result in more soul- searching. In the symposium by a group of biomedical journal editors published in the Annals of Internal Medicine in 1986 it was noted that most of the cases of scientific misconduct occur in very large laboratories which publish many papers each year. Secondly, as was pointed out in the symposium that I edited for the

FASEB Journal in 1989, large group research efforts which result in multi-authored publications, tend to dilute the feelings of responsibility by each of the individual authors. It was also noted by many that while laboratory studies may be easy to replicate (although at some expense of time and money), clinical studies are not and are usually - especially large studies intended for judging drug efficacy, and safety for FDA approval - never replicated in detail. The public clearly does not distinguish one type of science from another in their concern for authoritative results. Surprisingly, we have seen that controversies on arcane aspects of immunobiology are viewed with some of the same concern focused on controversies involving breast cancer treatment protocols.

The first major formal response of the scientific community to the issue of scientific misconduct, and in my opinion still among the best, was the Institute of Medicine (IOM) report, "The Responsible Conduct of Research in the Health Sciences," issued in 1989, under the chairmanship of Dr. Arthur Rubenstein. I commend each of you to read it, especially its careful list of recommendations to the institutions involved, i.e., NIH, universities and research organizations and professional and scientific organizations and journals. The report clearly acknowledged the existence of problems for the scientific community related to scientific misconduct and, among other suggestions, proposed that each institution develop its own standards for the conduct of research. The thrust of these suggestions put responsibility clearly on the major institutions involved in supporting and overseeing science as well as individual scientists. The report was viewed with considerable discomfort by the scientific community and was, as far as I can tell, subject to relatively little discussion.

The topic, however, would not go away and in 1992 the National Academy of Sciences / National Academy of Engineering / Institute of Medicine issued a report "Responsible Science: Ensuring the Integrity of the Research Process" which is still the most comprehensive treatment available from an official body on the subject. The report suggested that a distinction be made among three types of behaviors: 1) misconduct in science, 2) questionable research practices, and 3) other types of misconduct. The definition of misconduct in science was given as "fabrication, falsification, or plagiarism in proposing, performing, or reporting research." The phrase "other practices that ... deviate ..." in the federal rules was omitted. However, a new category of "questionable research practices," was defined as "actions that violate traditional values in the research enterprise and that may be detrimental to the research process." Failure to retain data, inadequate records, honorary authorship, premature release of results to the public and other actions of this type were singled out but shielded from jurisdiction in scientific misconduct proceedings. The third category of "other types of misconduct" included financial irregularities, sexual harassment, conflicts of interest and other behavior covered by existing rules and regulations.

The most important recommendations of the report were 1) "individual scientists [emphasis added] in cooperation with officials of research institutions should accept formal responsibility for ensuring the integrity of the research process," 2) scientists and research institutions should have educational programs that foster awareness of concerns, 3) institutions should consider voluntary guidelines for the conduct of research, 4) a common framework of definitions of misconduct be adopted by institutions and the government, as well as common policies and procedures

for handling allegations of misconduct and 5) an independent federal Scientific Integrity Advisory Board be created.

This report was more widely discussed than its predecessor IOM report but was felt by many to be much weaker than that report. There was some controversy about the restricted definition of misconduct and about the creation of the new category of "questionable research practices." There was more criticism, however, of the failure to recommend more strongly concerning conduct guidelines and the existence of problems of conflicts of interest, as well as the vagueness concerning procedures of review of allegations and even the nature of the proposed Scientific Integrity Advisory Board. In my opinion the major accomplishment of this report was that the scientific establishment as a whole grappled with this unpleasant issue for the first time; the major disappointment was the equivocation on many issues. In general, one reads the report as still being very defensive towards the institutions and structures of the scientific community. Note that it focuses much more than the IOM report on individual rather than institutional responsibility.

The NIH Intramural Research Program felt, as these issues evolved in the late 1980's, that it had an institutional responsibility to define a set of guidelines for the conduct of research that could be used as a basis of discussion, as well as education, of scientists, especially those in training. Dr. Edward Rall, then Deputy Director of Intramural Research, appointed a sub-committee of the NIH Scientific Directors, under the Chairmanship of Dr. Edward Korn to draft such guidelines. These were initially issued in April 1990 and have subsequently been revised and reissued several times (the

latest in January 1997). The current version, Guidelines for the Conduct of Research in the Intramural Research Program at NIH, is a 17 page booklet divided into the nine sections shown in Figure 2. As stated in the Introduction, the Guidelines were "developed to promote high ethical standards in the conduct of research by intramural scientists at NIH...and not to codify a set of rules." In particular they were intended to provide a framework for the fair and open conduct of research without inhibiting scientific freedom and creativity. The writers of the Guidelines also attempted to be cognizant of the major differences in commonly acceptable behavior among different scientific disciplines. In discussions with scientists in other disciplines, such as mathematics and physics, it has become clear to me that conduct accepted in the biomedical sciences - especially related to the competitiveness of these fields - would be totally unacceptable to individuals in the physical sciences. For example, oral communications are given much lower weight and priority in the biomedical sciences than in the physical sciences. As a result of these differences, codifying even these general principles has not been easy and it is expected that they will continue to evolve.

Up until now the Guidelines have found their greatest use at NIH (and in the other institutions that have developed their own guidelines), I believe, as a framework for the education of staff scientists and trainees in conduct issues through occasional discussion sessions and more formal courses. Some of us, however, have been concerned that these sessions not become - or be perceived - as similar to those involving Mao's "little red book" during the Chinese Cultural Revolution. The outspokenness of most individual

scientists gives us confidence that this will not happen. The text of the current (1997) edition of the NIH Guidelines is appended for closer study.

The recent publication of several textbooks (see Suggested Reading list) and the evolution of formal courses in this subject at many institutions is also to be noted. In addition in 1996, the NIH created a Committee on Scientific Conduct and Ethics to help set policies on these issues as well as to set in place mechanisms for teaching the principles of scientific conduct and to establish mechanisms to resolve specific cases, including the creation of an "ombudsman" to consider problematic situations related to scientific conduct.

In the immediate future, I think that several unresolved issues have yet to play out as the public and the scientific community evolve toward a consensus on the conduct issues discussed above. First, the scientific community generally appear to hope that the definition of misconduct will be narrowed - as suggested in the NAS/NAE/IOM report - and that the other categories of misbehavior be explicitly recognized and sharply differentiated from scientific misconduct-related issues. It is widely felt, equally by lawyers as by scientists, that the "or other practices that seriously deviate" phrase is so vague as to be useless and could well become a threat to scientific innovation. Dr. Howard Schachman, of the University of California at Berkeley, has been particularly articulate in pointing out the dangers of vague regulations, especially their potential of misuse by officials. The author of this article has observed several attempts by scientists involved in authorship disputes to use allegations of scientific misconduct as subterfuges for other objectives.

Complicating matters, however, is that in 1993 - as a result of a Congressional Mandate - DHHS created a Commission on Research Integrity, which in November 1995, submitted yet another report. The Commission's report, "Integrity and Misconduct in Research" suggested that definition be based on "the fundamental principle that scientists be truthful and fair in the conduct of research and the dissemination of its results." In particular, the concepts of misappropriation, interference, and misrepresentation (MIM) were introduced as canonical examples of potential research misconduct. In addition, special concerns to the rights of "whistleblowers" and administrative processes and investigations for dealing with misconduct issues were formulated. This report had a largely negative response by the scientific community and the DHHS established a federal "implementation group" which recommended, in general, a cautious response to the report. Neither the Secretary of DHHS nor Congress (with potential legislation) has acted so far on the report. The totally new approach to the definition of research misconduct has caused much confusion among those dealing with these issues.

Second, the problems of individual and institutional conflicts of interest (especially financial) must, I believe, be handled more frankly and honestly than has been the case heretofore. If we believe that the importance of the scientific method in advancing our understanding of the universe and ourselves, including health, is related to its relative objectivity, as compared to other approaches, then the scientific community must ensure minimal interference with striving for this objectivity. Whereas intellectual and personal conflicts of interest can usually be recognized, hidden financial ones can markedly influence conclusions in undetectable ways. For these reasons

disclosure of all relevant financial relationships would appear to be essential at all stages of planning, executing, analyzing, reporting, and judging scientific work. Whether disclosure is sufficient to assuage concerns about the impact of financial conflicts of interest, is however, itself debatable. Interestingly it should be realized that the conflict of interest issue applies to the institutions that employ scientists - even non-profit and governmental, as well as those for profit - as well as the scientists themselves. The interest of these institutions in continuing to receive the overhead from federal grants, patent or licensing royalties, or the prestige of being the employers of important scientists creates conflicts of interest but at least these should be apparent to most observers. Medical journals have been at the forefront in efforts to force disclosure of financial conflicts of interest, and even limit the activities (such as in writing review articles) of those involved. Some scientific societies have followed these precedents but attempts to enunciate these in federal regulations have been controversial and stymied for years.

It is important to realize that the existence of explicit or implicit conflicts of interest apply to an understanding of the way in which scientific institutions - government or private - have in general reacted to the scientific conduct issues discussed in this paper during the last two decades. Clearly these concerns need further discussion before a consensus for action can be approached. The implicit tension as to the relative responsibilities of individual scientists versus their institutions with regard to scientific conduct issues, a theme of this review, is a largely silent but significant part of this debate. To make individuals primarily responsible is obviously appealing at first glance but it tends to promote scapegoating and the continuation of institutional practices that may themselves be corrupt. Voluntary abnegation

of conflict of interest situations, for example, is unlikely to ever be sufficient. Although the behavior of individuals ultimately determines that of the enterprise, the organizational framework of science is well defined and unless these institutions take responsibility we are all at the mercy of a few "entrepreneurs".

In conclusion I would like to make three points. First, many cases involving allegations about scientific misconduct have gone on for years, approaching a decade in several instances. Closure has seemed impossible in many of these cases. I think that this is because these controversies are frequently being fought simultaneously in as many as five venues - the scientific arena, the administrative processes, the law courts, the Congressional hearing rooms, and the media. Each has its own rules and goals, and these are frequently contradictory. As long as this situation persists, I think the scientific misconduct issue - especially when it involves factors that impact on public health - will always be a hypersensitive issue waiting to erupt with untold consequences.

Second, we must be careful that our concerns about scientific conduct issues not lead to changes in those mechanisms that underlie scientific creativity as well as objectivity. Periods of scientific flowering have been very episodic and moved rapidly from one country or culture to another as societies changed. Thus we think specifically of the accomplishments of ancient Egypt, classical Greece, medieval Arabia, Ming China, revolutionary France, industrial Germany and post-World War II United States. We must be careful that the ways in which we address the problems that I have discussed are not so heavy handed that the golden age of American science in

the last fifty years is not eclipsed. The students and post-doctoral fellows who are flocking to the United States for training could soon be migrating to other countries.

The last point I make concerns what we as individual scientists can do to impact on these issues positively. Clearly we and our institutions must value intellectual honesty above other considerations in all our actions. We must also explain and defend the process of science itself, i.e. the scientific method. The unacceptable behavior of a few does not invalidate the success and importance of the methods of science, especially the procedures and conventions developed over the last 500 years. However, we obviously must not bury our heads in the sand and should continue to make personal and organizational changes so that this edifice is not endangered by a few cases of scandalous behavior. The public must also understand that error and controversy are the hallmarks of normal science conducted using the scientific method, not the exception. To this end we have a continuing responsibility to educate the public - including the media and especially those in school or university - in the history and approaches of the scientific method, as well as in the results of that science in both pure and applied disciplines.

Figure 1

"FINAL RULE"

Responsibilities of PHS Awardee and Applicant Institutions for Dealing with and Reporting Possible Misconduct in Science (54 *Federal Register* 32446, August 8, 1989).

1. Misconduct in science is defined as fabrication, falsification, plagiarism, or other practices that seriously deviate from those that are commonly accepted within the scientific community for proposing, conducting, or reporting research. It does not include honest error or honest differences in interpretations or judgments of data.

2. Creates Office of Scientific Integrity in the OD, NIH, and Office of Scientific Integrity Review in OASH, DHHS.

3. Each institution supported by the PHS must have relevant administrative processes in place for review of allegations of misconduct.

Figure 2

Guidelines for the
CONDUCT OF RESEARCH
in the Intramural Research Programs at the NIH

(1997)

Guidelines for the Conduct of Research at the National Institutes of Health

PREFACE

The Guidelines for the Conduct of Research expound the general principles governing the conduct of good science as practiced in the Intramural Research Programs at the National Institutes of Health. They address a need arising from the rapid growth of scientific knowledge, the increasing complexity and pace of research, and the influx of scientific trainees with diverse backgrounds. Accordingly, the Guidelines should assist both new and experienced investigators as they strive to safeguard the integrity of the research process.

The Guidelines were developed by the Scientific Directors of the Intramural Research Programs at the NIH and revised this year by the intramural scientists on the NIH Committee on Scientific Conduct and Ethics. General principles are set forth concerning the responsibilities of the research staff in the collection and recording of data, publication practices, authorship determination, peer review, confidentiality of information, collaborations, human subjects research, and financial conflicts of interest.

It is important that every investigator involved in research at NIH read, understand, and incorporate the Guidelines into everyday practice. The progress and excellence of NIH research is dependent on our vigilance in maintaining the highest quality of conduct in every aspect of science.

Michael M. Gottesman, M.D.
Deputy Director for Intramural Research, NIH

3rd Edition
January, 1997
The National Institutes of Health

Introduction

Scientists in the Intramural Research Program at the National Institutes of Health generally are responsible for conducting original research consonant with the goals of their individual Institutes and Divisions.

Intramural scientists at NIH, as all scientists, should be committed to the responsible use of the process known as the scientific method to seek new knowledge. While the general principles of the scientific method -formulation and testing of hypotheses, controlled observations or experiments, analysis and interpretation of data, and oral and written presentation of all of these components to scientific colleagues for discussion and further conclusions - are universal, their detailed application may differ in different scientific disciplines and in varying circumstances. All research staff in the Intramural Research Programs should maintain exemplary standards of intellectual honesty in formulating, conducting and presenting research, as befits the leadership role of the NIH.

These Guidelines were developed to promote high ethical standards in the conduct of research by intramural scientists at the NIH. It is the responsibility of each Laboratory or Branch Chief, and successive levels of supervisory individuals (especially Institute, Center

and Division Intramural Research Directors), to ensure that each NIH scientist is cognizant of these Guidelines and to resolve issues that may arise in their implementation.

These Guidelines complement, but are independent of, existing NIH regulations for the conduct of research such as those governing human subjects research, animal use, radiation, chemical and other safety issues, transgenic animals, and the Standards of Conduct that apply to all federal employees.

The formulation of these Guidelines is not meant to codify a set of rules, but rather to elucidate, increase awareness and stimulate discussion of patterns of scientific practice that have developed over many years and are followed by the vast majority of scientists, and to provide benchmarks when problems arise. Although no set of guidelines, or even explicit rules, can prevent willful scientific misconduct, it is hoped that formulation of these Guidelines will contribute to the continued clarification of the application of the scientific method in changing circumstances.

The public will ultimately judge the NIH by its adherence to high intellectual and ethical standards, as well as by its development and application of important new knowledge through scientific creativity.

Responsibilities of Research Supervisors and Trainees

Research training is a complex process, the central aspect of which is an extended period of research carried out under the supervision of an experienced scientist. This supervised research experience represents not merely performance of tasks assigned by the supervisor, but rather a process wherein the trainee takes on an increasingly independent role in the selection, conceptualization and execution of research projects. To prepare a young scientist for a successful career as a research investigator, the trainee should be provided with training in the necessary skills. It should be recognized that the trainee has unique needs relevant to career development.

In general a trainee will have a single primary supervisor but may also have other individuals who function as mentors for specific aspects of career development. It is the responsibility of the primary supervisor to provide a research environment in which the trainee has the opportunity to acquire both the conceptual and technical skills of the field. In this setting, the trainee should undertake a significant piece of research, chosen usually as the result of discussions between the mentor and the trainee, which has the potential to yield new knowledge of importance in that field. The mentor should supervise the trainee's progress closely and interact personally with the trainee on a regular basis to make the training experience meaningful. Supervisors and mentors should limit the number of trainees in their laboratory to the number for whom they can provide an appropriate experience.

There are certain specific aspects of the mentor-trainee relationship that deserve emphasis. First, training should impart to the trainee appropriate standards of scientific conduct both by instruction and by example. Second, mentors should be particularly diligent to involve trainees in research activities that contribute to their career development. Third, mentors should provide trainees with realistic appraisals of their performance and with advice about career development and opportunities.

Conversely, trainees have responsibilities to their supervisors and to their institutions. These responsibilities include adherence to these Guidelines, applicable rules, and programmatic constraints related to the needs of the laboratory and institute. The same

standards of professionalism and collegiality apply to trainees as to their supervisors and mentors.

Data Management

Research data, including detailed experimental protocols, all primary data, and procedures of reduction and analysis are the essential components of scientific progress. Scientific integrity is inseparable from meticulous attention to the acquisition and maintenance of these research data.

The results of research should be carefully recorded in a form that will allow continuous access for analysis and review. Attention should be given to annotating and indexing notebooks and documenting computerized information to facilitate detailed review of data. All data, even from observations and experiments not directly leading to publication, should be treated comparably. All research data should be available to scientific collaborators and supervisors for immediate review, consistent with requirements of confidentiality. Investigators should be aware that research data are legal documents for purposes such as establishing patent rights or when the veracity of published results is challenged and the data are subject to subpoena by congressional committees and the courts.

Research data, including the primary experimental results, should be retained for a sufficient period to allow analysis and repetition by others of published material resulting from those data. In general, five to seven years is specified as the minimum period of retention but this may vary under different circumstances.

Notebooks, other research data, and supporting materials, such as unique reagents, belong to the National Institutes of Health, and should be maintained and made available, in general, by the Laboratory in which they were developed. Departing investigators may take copies of notebooks or other data for further work. Under special circumstances, such as when required for continuation of research, departing investigators may take primary data or unique reagents with them if adequate arrangements for their safekeeping and availability to others are documented by the appropriate Institute, Center or Division official.

Data management, including the decision to publish, is the responsibility of the principal investigator. After publication, the research data and any unique reagents that form the basis of that communication should be made available promptly and completely to all responsible scientists seeking further information. Exceptions may be necessary to maintain confidentiality of clinical data or if unique materials were obtained under agreements that preclude their dissemination.

Publication Practices

Publication of results is an integral and essential component of research. Other than presentation at scientific meetings, publication in a scientific journal should normally be the mechanism for the first public disclosure of new findings. Exceptions may be appropriate when serious public health or safety issues are involved. Although appropriately considered the end point of a particular research project, publication is also the beginning of a process in which the scientific community at large can assess, correct and further develop any particular set of results.

Timely publication of new and significant results is important for the progress of science, but fragmentary publication of the results of a scientific investigation or multiple

publications of the same or similar data are inappropriate. Each publication should make a substantial contribution to its field. As a corollary to this principle, tenure appointments and promotions should be based on the importance of the scientific accomplishments and not on the number of publications in which those accomplishments were reported.

Each paper should contain sufficient information for the informed reader to assess its validity. The principal method of scientific verification, however, is not review of submitted or published papers, but the ability of others to replicate the results. Therefore, each paper should contain all the information that would be necessary for scientific peers of the authors to repeat the experiments. Essential data that are not normally included in the published paper, e.g. nucleic acid and protein sequences and crystallographic information, should be deposited in the appropriate public data base. This principle also requires that any unique materials (e.g. monoclonal antibodies, bacterial strains, mutant cell lines), analytical amounts of scarce reagents and unpublished data (e.g. protein or nucleic acid sequences) that are essential for repetition of the published experiments be made available to other qualified scientists. It is not necessary to provide materials (such as proteins) that others can prepare by published procedures, or materials (such as polyclonal antisera) that may be in limited supply.

Authorship

Authorship refers to the listing of names of participants in all communications, oral and written, of experimental results and their interpretation to scientific colleagues. Authorship is the fulfillment of the responsibility to communicate research results to the scientific community for external evaluation.

Authorship is also the primary mechanism for determining the allocation of credit for scientific advances and thus the primary basis for assessing a scientist's contributions to developing new knowledge. As such, it potentially conveys great benefit, as well as responsibility. For each individual the privilege of authorship should be based on a significant contribution to the conceptualization, design, execution, and/or interpretation of the research study, as well as a willingness to assume responsibility for the study. Individuals who do not meet these criteria but who have assisted the research by their encouragement and advice or by providing space, financial support, reagents, occasional analyses or patient material should be acknowledged in the text but not be authors.

Because of the variation in detailed practices among disciplines, no universal set of standards can easily be formulated. It is expected, however, that each research group and Laboratory or Branch will freely discuss and resolve questions of authorship before and during the course of a study. Further, each author should review fully material that is to be presented in public forums or submitted (originally or in revision) for publication. Each author should be willing to support the general conclusions of the study.

The submitting author should be considered the primary author with the additional responsibilities of coordinating the completion and submission of the work, satisfying pertinent rules of submission, and coordinating responses of the group to inquiries or challenges. The submitting author should assure that the contributions of all collaborators are appropriately recognized and that each author has reviewed and authorized the submission of the manuscript in its original and revised forms. The recent practice of some journals of requiring approval signatures from each author before publication is an indication of the importance of fulfilling the above.

Peer Review and Priveleged Information

Peer review can be defined as expert critique of either a scientific treatise, such as an article prepared or submitted for publication, a research grant proposal, a clinical research protocol, or of an investigator's research program, as in a site visit. Peer review is an essential component of the conduct of science. Decisions on the funding of research proposals and on the publication of experimental results must be based on thorough, fair and objective evaluations by recognized experts. Therefore, although it is often difficult and time-consuming, scientists have an obligation to participate in the peer review process and, in doing so, they make an important contribution to science.

Peer review requires that the reviewer be expert in the subject under review. The reviewer, however, should avoid any real or perceived conflict of interest that might arise because of a direct competitive, collaborative or other close relationship with one or more of the authors of the material under review. Normally, such a conflict of interest would require a decision not to participate in the review process and to return any material unread.

The review must be objective. It should thus be based solely on scientific evaluation of the material under review within the context of published information and should not be influenced by scientific information not publicly available.

All material under review is privileged information. It should not be used to the benefit of the reviewer unless it previously has been made public. It should not be shared with anyone unless necessary to the review process, in which case the names of those with whom the information was shared should be made known to those managing the review process. Material under review should not be copied and retained or used in any manner by the reviewer unless specifically permitted by the journal or reviewing organization and the author.

Collaborations

Research collaborations frequently facilitate progress and generally should be encouraged. It is advisable that the ground rules for collaborations, including eventual authorship issues, be discussed openly among all participants from the beginning. Whenever collaborations involve the exchange of materials between NIH scientists and scientists external to NIH, a Material Transfer Agreement (MTA) or other formal written agreements may be necessary. Information about such agreements and other relevant mechanisms, such as licensing or patenting discoveries, may be obtained from each ICD's Technology Development Coordinator or the NIH Office of Technology Transfer.

Human Subjects Research

Clinical research, for the purposes of these Guidelines, is defined as research performed on human subjects or on material or information obtained from human subjects as a part of human experimentation. All of the topics covered in the Guidelines apply to the conduct of clinical research; clinical research, however, entails further responsibilities for investigators.

The preparation of a written research protocol ("Clinical Research Protocol") according to existing guidelines prior to commencing studies is almost always required. By virtue of its various sections governing background; patient eligibility and confidentiality; data to be collected; mechanism of data storage, retrieval, statistical analysis and reporting; and

identification of the principal and associate investigators, the Clinical Research Protocol provides a highly codified mechanism covering most of the topics covered elsewhere in the Guidelines. The Clinical Research Protocol is generally widely circulated for comment, review and approval. It should be scrupulously adhered to in the conduct of the research. The ideas of the investigators who prepared the protocol should be protected by all who review the document.

Those using materials obtained by others from patients or volunteers are responsible for assuring themselves that the materials have been collected with due regard for principles of informed consent and protection of human subjects from research risk. Normally, this is satisfied by a protocol approved by a human subjects committee of the institution at which the materials were obtained.

The supervision of trainees in the conduct of clinical investigation is complex . Often the trainees are in fellowship training programs leading to specialty or subspecialty certifications as well as in research training programs. Thus, they should be educated in general and specific medical management issues as well as in the conduct of research. The process of data gathering, storage, and retention can also be complex in clinical research which sometimes cannot easily be repeated. The principal investigator is responsible for the quality and maintenance of the records and for the training and oversight of all personnel involved in data collection.

Epidemiologic research involves the study of the presence or absence of disease in groups of individuals. Certain aspects of epidemiologic research deserve special mention. Although an epidemiologist does not normally assume responsibility for a patient's care, it is the responsibility of the epidemiologist to ensure that the investigation does not interfere with the clinical care of any patient. Also, data on diseases, habits or behavior should not be published or presented in a way that allows identification of any particular individual, family or community. In addition, even though it is the practice of some journals not to publish research findings that have been partially released to the public, it may be necessary for reasons of immediate public health concerns to report the findings of epidemiologic research to the study participants and to health officials before the study has been completed; the health and safety of the public has precedence.

Development and review of detailed protocols are as important in epidemiologic research as in clinical research and any other health science. However, the time for protocol development and review may be appropriately shortened in circumstances such as the investigation of acute epidemic or outbreak situations where the epidemiologic investigation may provide data of crucial importance to the identification and mitigation of a threat to public health. Nevertheless, even in these situations, systematic planning is of great importance and the investigator should make every attempt to formalize the study design in a written document and have it peer-reviewed before the research is begun.*

Financial Conflicts of Interest

Potential conflicts of interest due to financial involvements with commercial institutions may not be recognized by others unless specific information is provided. Therefore, the scientist should disclose all relevant financial relationships, including those of the scientist's immediate family, to the Institute, Center or Division during the planning, conducting and reporting of research studies, to funding agencies before participating in peer review of applications for research support, to meeting organizers before presentation of results, to journal editors when submitting or refereeing any material for publication, and in all written communications and oral presentations

Concluding Statement

These Guidelines are not intended to address issues of misconduct nor to establish rules or regulations. Rather, their purpose is to provide a framework for the fair and open conduct of research without inhibiting scientific freedom and creativity.

*The section on epidemiological research is adapted from the GUIDELINES FOR THE CONDUCT OF RESEARCH WITHIN THE PUBLIC HEALTH SERVICE, January 1, 1992.

These Guidelines were originally prepared by a Committee appointed by the NIH Scientific Directors. This third edition was prepared by the NIH Committee on Scientific Conduct and Ethics and approved by the NIH Scientific Directors

Suggested Reading

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February 12, 1996
Alan N. Schechter, M.D.
Case One

Case for Discussion in Scientific Ethics Session

Drs. X. and Y. are two of the major competitors in a rapidly developing field of research that may lead to a new diagnostic method for certain human cancers.

Dr. X. submits a paper to Journal A., which sends it to Dr. Y. as one of the referees.

Dr. Y. shows the paper to several of his co-workers and discusses it with them before returning the manuscript to the Journal with a recommendation that several further experiments should be reported before it might be accepted for publication.

One year later Dr. Y. submits a paper to Journal B. describing results closely related to those in the first manuscript and also noting their relevance to the diagnosis of certain cancers. He does not mention Dr. X.'s work (which has not yet been published).

Discuss your evaluation of the ethical issues in this scenario.

(Adapted from a case presented by Dr. David Klein.)

February 12, 1996
Alan N. Schechter, M.D.
Case Two

Case for Discussion in Scientific Ethics Session

Dr. B., a physician, is the Principal Investigator on an NIH funded Program Project Grant, at a university medical center, for the study of the treatment of OM in children. Dr. C., is a biomedical engineer who is Research Director of the project, has been involved with it for more than a decade and is first author on many of its publications.

Drs. B. and C. have a dispute on whether the results with a certain drug show that it is effective in treating OM. Dr. B. submits a manuscript to Journal N. claiming effectiveness; Dr. C. submits a manuscript based on same study concluding the opposite. The journal queries the university, which indicates that Dr. B.'s manuscript is "official"; Journal N. publishes that version. Several years later Journal A. publishes Dr. C.'s manuscript after many acrimonious private and public exchanges among all involved.

The university institutes misconduct proceedings against Dr. C. In turn, Dr. C., brings charges of "censorship" against the university, and conflict of interest against Dr. B., because the study was significantly supported by funds from the manufacturer of the drugs without indication of this.

This case raises the following questions:

1) Who "owns" the data from a collaborative study?

2) Can a coinvestigator dissent in publication for the views of his colleagues, in what form, and in what forum?

3) Were the events as described cause for an investigation or finding of misconduct? What recourse does the dissenter have?

4) Did the university engage in "censorship?"

5) Did the editor of N. handle his responsibilities adequately?

6) Is support of the study by a drug company an important issue?

(Adapted from case report of Dr. R. Asofsky.)

January 16, 1996
Alan N. Schechter, M.D.
Case Three

Case for Discussion in Scientific Ethics Session

A major portion of a student's draft doctoral dissertation is being prepared as a manuscript for submission to a peer-reviewed journal, as well as for inclusion in the final thesis. The mentor has suggested additional experiments for the student to do, including the suggestion that the tow recombinant proteins under study be analyzed by 2D nuclear magnetic resonance spectroscopy (NMR). She suggests that this be done collaboratively with a biophysical chemist in another department. Both the mentor and the student agree that this would be a significant contribution and would add considerable strength to the work. The collaboration is set up over the course of the following two weeks. The mentor then tells the student that she would like him to audit a graduate level course in biophysical techniques being offered in the next semester. The mentor feels strongly that the student should have reasonable command of NMR techniques if the student's paper is going to contain NMR data. The student thought he was within a few ..... of completing all of his degree requirements and he strongly objects to the mentor's suggestion, stating that he can gain the necessary working knowledge to defend the collaboratively obtained NMR data by reading on his own. Comment on this situation. What are the responsibilities of the biophysical chemist who will do the NMR studies? Are there other alternatives you can suggest in this situation. (Adapted from Macrina, F.L., Scientific Integrity: An Introductory Test with Cases, ASM Press, Washington, D.C. 1995.)